

a single donor source of antiserum. Each of these tests shall be conducted and interpreted independently, and any discrepancy between the results of these two tests shall be resolved by testing with at least one additional antiserum before concluding that the antigen is present or absent. Where fewer than three donor sources of an antibody specificity are available, test discrepancies shall be resolved in accordance with the manufacturer's biologics license application. Group O Reagent Red Blood Cells used in the detection or identification of unexpected antibodies shall include at least the following common antigens in each lot of the product: D, C, E, \bar{c} , e, K, k, Fy^a, Fy^b, Jk^a, Jk^b, Le^a, Le^b, P₁, M, N, S, and S.

[52 FR 37450, Oct. 7, 1987, as amended at 55 FR 11013, Mar. 26, 1990; 64 FR 56454, Oct. 20, 1999]

§ 660.34 Processing.

(a) *Processing method.* The processing method shall be one that has been shown to yield consistently a product that is capable of detecting, throughout the dating period, alloantibodies corresponding to all required blood group antigens specified in the labeling as present.

(b) *Products prepared from pooled red blood cells.* If the product is recommended for the detection of unexpected antibodies, the pool shall be prepared by combining equal amounts of cells from no more than two donors. Umbilical cord cells are exempt from this requirement. Pooled cells shall not be recommended for pretransfusion tests, done in lieu of a major cross-match, to detect unexpected antibodies in patients' samples.

(c) *Absence of antibodies.* Each lot of final product shall be free of demonstrable antibodies, including anti-A and anti-B, unless the package insert and container label include instructions to wash the cells before use. The final product shall also be direct antiglobulin test negative when tested with polyspecific anti-human globulin.

(d) *Final container.* The final containers used for each lot of product shall be clean and shall permit observation of the contents for hemolysis or a change in color. The final container label, container cap, and dropper bulb

of a Reagent Red Blood Cell product may be color-coded with a visual match to a specific color approved by the Director, Center for Biologics Evaluation and Research.

(e) *Date of manufacture.* The date of manufacture of the product shall be the date that the blood is withdrawn from the donor or obtained from umbilical cords. The period during which the reagent red blood cell source material is kept by the manufacturer in storage in a frozen state at -65°C or colder is excluded from the dating period. If the product consists of red blood cells from two or more donors, the date of manufacture of the final product shall be the date of withdrawal of blood from the donor of the oldest constituent blood. When a product consists of more than one container, e.g., cell panel, the date of manufacture of each container of the product shall be the earliest date that blood was withdrawn from a donor for any container of the product.

(f) *Retention samples.* Retention samples shall be maintained as required by § 600.13 of this chapter, except that samples must be retained only throughout the dating period of the product.

[52 FR 37450, Oct. 7, 1987, as amended at 55 FR 11013, Mar. 26, 1990; 67 FR 9587, Mar. 4, 2002]

§ 660.35 Labeling.

In addition to the items required by § 809.10 of this chapter and other applicable labeling provisions of this chapter, the following information shall be included in the labeling:

(a)(1) A logo or company name may be placed on the final container label, however, the logo or company name shall be located along the bottom or end of the label, outside of the main panel.

(2) If washing the cells is required by the manufacturer, the container label shall include appropriate instructions; if the cells should not be washed before use, e.g., if washing will adversely affect the product, the package insert shall explain.

(b) The container label of Group O cells shall state:

"FOR USE IN DETECTION OF UNEXPECTED ANTIBODIES" or "FOR USE IN IDENTIFICATION OF UNEXPECTED ANTIBODIES" or "NOT FOR USE IN DETECTION

OR IDENTIFICATION OF UNEXPECTED ANTIBODIES”.

(c) Except as provided in this section, the container and package labels shall state the percentage of red blood cells in the suspension either as a discrete figure with a variance of more than ± 1 percentage unit or as a range the extremes of which differ by no more than 2 percentage units. If the stated red blood cell concentration is less than 2 percent, the variance shall be no more than ± 0.5 percentage unit.

(d) The words “pooled cells” shall appear on the container and package labels of products prepared from pooled cells. The package label or package insert shall state that pooled cells are not recommended for pretransfusion tests, done in lieu of a major cross-match, to detect unexpected antibodies in patients’ samples.

(e) The package insert of a pooled product intended for detection of unexpected antibodies shall identify the number of donors contributing to the pool. Products designed exclusively for ABO Serum Grouping and umbilical cord cells need not identify the number of donors in the pool.

(f) When the product is a multicontainer product, e.g., a cell panel, the container label and package label shall be assigned the same identifying lot number, and shall also bear a number or symbol to distinguish one container from another. Such number or symbol shall also appear on the antigenic constitution matrix.

(g) The package label or package insert shall state the blood group antigens that have been tested for and found present or absent on the cells of each donor, or refer to such information in an accompanying antigenic constitution matrix. Cells for ABO Serum Grouping are exempt from this requirement. The package insert or antigen constitution matrix shall list each of the antigens tested with only one source of antibody.

(h) The package label or package insert shall bear the cautionary statement: “The reactivity of the product may decrease during the dating period.”

(i) The package insert of a product intended for the detection or identification of unexpected antibodies shall

note that the rate at which antigen reactivity (e.g., agglutinability) is lost is partially dependent upon individual donor characteristics that are neither controlled nor predicted by the manufacturer.

(j) The package insert shall provide adequate directions for use.

(k) The package insert shall bear the statement:

“CAUTION: ALL BLOOD PRODUCTS SHOULD BE TREATED AS POTENTIALLY INFECTIOUS. SOURCE MATERIAL FROM WHICH THIS PRODUCT WAS DERIVED WAS FOUND NEGATIVE WHEN TESTED IN ACCORDANCE WITH CURRENT FDA REQUIRED TESTS. NO KNOWN TEST METHODS CAN OFFER ASSURANCE THAT PRODUCTS DERIVED FROM HUMAN BLOOD WILL NOT TRANSMIT INFECTIOUS AGENTS.”

(l) The package insert or the antigenic constitution matrix for each lot of product shall specify the date of manufacture or the length of the dating period.

(m) Manufacturers shall identify with a permanent donor code in the product labeling each donor of peripheral blood used for detection or identification of unexpected antibodies.

[52 FR 37450, Oct. 7, 1987, as amended at 67 FR 9587, Mar. 4, 2002]

§ 660.36 Samples and protocols.

(a) The following shall be submitted to the Center for Biologics Evaluation and Research Sample Custodian (ATTN: HFM-672) (see mailing addresses in § 600.2 of this chapter), within 30 days after each routine establishment inspection by FDA.

(1) From a lot of final product, samples from a cell panel intended for identification of unexpected antibodies. The sample shall be packaged as for distribution and shall have at least 14 days remaining in the dating period when shipped to the Center for Biologics Evaluation and Research.

(2) A protocol which shall include the following:

(i) Complete test records of at least two donors of the samples submitted, including original and confirmation phenotyping records.

(ii) Bleeding records or receipt records which indicate collection date, volume, and HBsAg test results.